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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,902	11/17/2000	John James Donnelly	1627.003	5612

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Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 08/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/715,902	Applicant(s) DONNELLY ET AL.	
	Examiner Anne Marie Wehbe	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6,7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response to the restriction/election received on 5/28/02 has been entered. Claims 1-31 are pending in the instant application. Applicant's election with traverse of the subject matter of group I, claims 1-23 and 29-31 is acknowledged. Claims 24-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9. Claims 1-23 and 29-31 are currently under examination. An action on the merits follows.

Election/Restriction

As noted above, the applicants have elected the subject matter of group I, claims 1-23 and 29-31 with traverse. The traversal is on the ground(s) that search and examination of the entire application would not present an undue burden. This is not found persuasive because the restriction requirement mailed on 3/26/02, paper no. 8, clearly states that the transfected antigen presenting cells can be used in methods substantially different from stimulating T cells in vitro, such as their use to directly induce immune responses in vivo, or to produce heterologous protein. Further, the methods of invention II require the use of isolated T cells which are not required for the methods of invention I. Therefore, because these inventions are distinct for the reasons given

above and have acquired a separate status in the art because of their recognized divergent subject matter, and different search requirements, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-23 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/24447, 7/10/97, hereafter referred to as Song et al., in view of US Patent No. 5,783,567

(7/21/98), hereafter referred to as Hedley et al., and further in view of Fattal et al. (1998) J. Controlled Rel., Vol. 53, 137-143. The applicant claims methods of transfecting dendritic cells comprising incubating dendritic cells with a transfection agent comprising a polynucleotide and microparticles comprising a biodegradable polymer and a cationic detergent, the dendritic cells made using this method, and method of producing an immune response in a subject by administering said dendritic cells directly or parenterally. The applicant further claims wherein the dendritic cells are bone-marrow derived or blood derived, or wherein the polymer is poly (alpha-hydroxy acid), poly(lactide), poly (D, L-lactide-co-glycolide) or a copolymer of D, L lactide and caprolactone. The applicant also claims wherein the polynucleotide is a plasmid encoding a viral antigen from HIV or a tumor antigen, wherein the dendritic cells are cultured prior to transfection, or wherein the cationic detergent is CTAB or cetrimide.

Song et al. teaches methods of transfecting dendritic cells ex vivo or in vitro with a gene delivery vehicle comprising DNA encoding an antigen such as a tumor antigen or HIV antigen, and use of said transfected dendritic cells to induce an immune response against the expressed antigen in vivo (Song et al., pages 2, 3, and 18-20). Song et al. teaches that the transfected dendritic cells can be administered to a vertebrate parenterally or by direct injection, and that the dendritic cells can be derived from bone marrow and cultured for at least 7 days prior to transfection (Song et al., pages 26 and 39). Song et al. also teaches wherein the DNA encoding an antigen is a plasmid DNA (Song et al., page 18).

Song et al. differs from the instant invention by not specifically teaching the use of the combination of polynucleotides, biodegradable polymers, and cationic detergents as a gene delivery vehicle for dendritic cells. Song et al. however does teach that numerous gene delivery vehicles can be successfully utilized to transfect dendritic cells including the use of plasmid/liposomes, and plasmid combined with cationic condensing agents. Hedley et al. supplements Song et al. by teaching the use of microspheres comprising biodegradable polymers and DNA plasmids to introduce and express antigens encoded by the plasmids in antigen presenting cells such as macrophages and dendritic cells both in vitro and in vivo for the purpose of stimulating antigen specific immune responses (Hedley et al., columns 2-3 and 7-8). Hedley et al. further teaches that numerous biodegradable polymers and copolymers can be used to form the microspheres including poly(lactide) and poly (caprolactone) (Hedley et al., columns 10-11). As a preferred embodiment, Hedley et al. teaches the use of the copolymer (D, L-lactide-co-glycolide) (Hedley et al., column 11). Hedley et al. further teaches the preparation of microparticles comprising plasmid DNA which have a size of about 1 micron (Hedley et al., column 14). Hedley et al. further provides motivation for introducing plasmid DNA encoding an antigen to dendritic cells and macrophages by teaching that DNA combined with biodegradable microparticles is efficiently phagocytosed by APCs and is an effective means for introducing nucleic acids into these cells (Hedley et al., column 8, lines 13-49). Thus, based on the motivation to introduce nucleic acids into macrophages and dendritic cells using biodegradable polymers as taught by Hedley et al., it would have been *prima facie* obvious to the skilled artisan to use biodegradable

particles and plasmid DNA as the gene delivery vehicle in the methods of transfecting dendritic cells and methods of immunizing taught by Song et al. Further, based on the efficiency of phagocytosis of biodegradable particles taught by Hedley et al., the skilled artisan would have had a reasonable expectation of success in using biodegradable particles to deliver polynucleotides to dendritic cells in vitro or in vivo.

Both Song et al. and Hedley et al. differ from the instant invention in that they do not teach that use of microparticles containing cationic detergent to transfect dendritic cells. Fattal et al. teaches that the association of oligonucleotides with particles comprised of biodegradable polymers is increased by the addition of cationic detergents such as CTAB (Fattal et al., pages 137 and 139, Figure 1). Fattal et al. further reports an increase in phagocytosis/endocytosis of nanoparticles made using a cationic detergent (Fattal et al., page 137). Thus, Fattal et al. provides motivation for including a cationic detergent such as CTAB in the preparation of transfection agents comprising biodegradable polymers and polynucleotides in order to increase the amount of polynucleotide associated with the polymer particles and increase the uptake of the microparticles by phagocytosis. In view of the motivation provided by Fattal et al. discussed above, it would have been *prima facie* obvious to the skilled artisan at the time of filing to include a cationic detergent in gene delivery vehicle comprising biodegradable polymers in order to increase the association of polynucleotide with the particle and to increase phagocytosis by the target cell. Further, the skilled artisan would have had a reasonable expectation of making and using a transfection agent comprising a polynucleotide and biodegradable polymer particles comprising a

cationic detergent to transfect dendritic cells based on the successful use of oligonucleotide nanoparticles comprising biodegradable polymer and CTAB taught by Fattal et al. to transfect cells in vitro and in vivo.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé